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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS  4  APR 04   STN AnaVist $500 visualization usage credit offered
 NEWS  5  MAY 10   CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  6  MAY 11   KOREAPAT updates resume
 NEWS  7  MAY 19   Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  9  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 11  JUN 26   TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 12  JUN 28   Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13  JUl 11   CHEMSAFE reloaded and enhanced
 NEWS 14  JUl 14   FSTA enhanced with Japanese patents
 NEWS 15  JUl 19   Coverage of Research Disclosure reinstated in DWPI

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 15:08:14 ON 07 AUG 2006

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 15:08:26 ON 07 AUG 2006
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STRUCTURE FILE UPDATES: 6 AUG 2006 HIGHEST RN 899126-84-2
DICTIONARY FILE UPDATES: 6 AUG 2006 HIGHEST RN 899126-84-2

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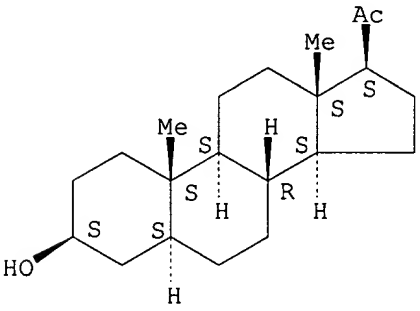
http://www.cas.org/ONLINE/UG/regprops.html

=> s allopregnanolone/cn
L1 2 ALLOPREGNANOLONE/CN

=> d str cn rn

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

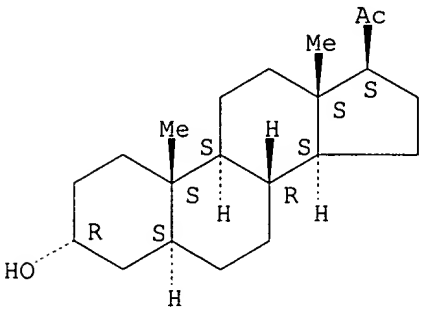
CN Pregnan-20-one, 3-hydroxy-, (3β,5α)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5α-Pregnan-20-one, 3β-hydroxy- (6CI, 8CI)
OTHER NAMES:
CN 3-Deoxo-3β-hydroxy-5α-dihydroprogesterone
CN 3β-Allopregnanolone
CN 3β-Hydroxy-5α,17β-pregnan-20-one
CN 3β-Hydroxy-5α-pregnan-20-one
CN 3β-Hydroxy-5α-tetrahydroprogesterone
CN 5α-Dihydropregnenolone
CN 5α-Pregnan-3β-ol-20-one
CN 5α-Pregnane-3β-ol-20-one
CN Allopregnan-3β-ol-20-one
CN Allopregnanolone
CN Epiallopregnanolone
CN Isopregnanolone

CN NSC 97078
CN U 0949
RN 516-55-2 REGISTRY

=> d L1 2 str cn rn

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Pregnan-20-one, 3-hydroxy-, (3α,5α)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5α-Pregnan-20-one, 3α-hydroxy- (6CI, 8CI)
OTHER NAMES:
CN (+)-3α-Hydroxy-5α-pregnan-20-one
CN (3α)-Allopregnanolone
CN 3α,5α-Pregnanolone
CN 3α,5α-Tetrahydroprogesterone
CN 3α,5α-THP
CN 3α-Hydroxy-5α-dihydroprogesterone
CN 3α-Hydroxy-5α-pregnan-20-one
CN 3α-Hydroxy-5α-pregnane-20-one
CN 5α-Pregnan-3α-ol-20-one
CN 5α-Pregnane-3α-ol-20-one
CN Allopregnan-3α-ol-20-one
CN Allopregnanolone
CN Allotetrahydroprogesterone
RN 516-54-1 REGISTRY

=> file caplus medline biosis embase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.44	9.65

FILE 'CAPLUS' ENTERED AT 15:09:32 ON 07 AUG 2006
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FILE 'MEDLINE' ENTERED AT 15:09:32 ON 07 AUG 2006

FILE 'BIOSIS' ENTERED AT 15:09:32 ON 07 AUG 2006

FILE 'EMBASE' ENTERED AT 15:09:32 ON 07 AUG 2006

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=> s 516-54-1
L2        2024 516-54-1

=> s 516-55-2
L3        1813 516-55-2

=> s allopregnanolone
L4        2595 ALLOPREGNANOLONE

=> s L2 or L3 or L4
L5        4367 L2 OR L3 OR L4

=> dup rem L5
PROCESSING IS APPROXIMATELY  36% COMPLETE FOR L5
PROCESSING IS APPROXIMATELY  74% COMPLETE FOR L5
PROCESSING COMPLETED FOR L5
L6         2457 DUP REM L5 (1910 DUPLICATES REMOVED)

=> s neurodegeneration
L7       31275 NEURODEGENERATION

=> s L6 and L7
L8           6 L6 AND L7

=> s traumatic injury
L9        9554 TRAUMATIC INJURY

=> s L6 and L9
L10          3 L6 AND L9

=> d 1-6 L8 ibib abs

L8   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2006:320931  CAPLUS
DOCUMENT NUMBER:         145:21261
TITLE:                   Neurosteroids in the brain neuron: biosynthesis,
                         action and medicinal impact on neurodegenerative
                         disease
AUTHOR(S):               Tsutsui, Kazuyoshi; Mellon, Synthia H.
CORPORATE SOURCE:        Laboratory of Brain Science, Faculty of Integrated
                         Arts and Sciences, Hiroshima University,
                         Higashi-Hiroshima, 739-8521, Japan
SOURCE:                  Central Nervous System Agents in Medicinal Chemistry
                         (2006), 6(1), 73-82
                         CODEN: CNSAC3; ISSN: 1871-5249
PUBLISHER:               Bentham Science Publishers Ltd.
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
AB   A review.  The brain has traditionally been considered to be a target site
     of peripheral steroid hormones.  By contrast, new findings over the past
     decade have shown that the brain itself also has the capability of forming
     steroids de novo from cholesterol, the so-called "neurosteroids".  To
     understand neurosteroid action in the brain, data on the regio- and
     temporal-specific synthesis of neurosteroids are needed.  Recently the
     Purkinje cell, a cerebellar neuron, has been identified as a major site
     for neurosteroid formation in the brain.  Since this discovery, diverse
     actions of neurosteroids are becoming clear.  The rat Purkinje cell
     actively synthesizes progesterone and 3α,5α-
     tetrahydroprogesterone (allopregnanolone) de novo from
     cholesterol during neonatal life, when cerebellar cortical formation
     occurs.  Estrogen formation in this neuron may also occur in the neonate.
     Both progesterone and estradiol promote dendritic growth, spinogenesis and
     synaptogenesis via each cognate nuclear receptor in Purkinje neurons.  We
```

have used the Niemann-Pick type C (NP-C) mouse as a model for understanding neurosteroid action in the brain. NP-C is an autosomal recessive, childhood neurodegenerative disease characterized by defective intracellular cholesterol trafficking, resulting in Purkinje cell degeneration, as well as neuronal degeneration in other regions. Brains from adult NP-C mice contain less allopregnanolone than wild-type brain. Administration of allopregnanolone to neonatal NP-C mice increases Purkinje cell survival and delays neurodegeneration. Thus neurosteroid replacement therapy appears to be useful in ameliorating progression of the disease. Here we summarize the advances made in our understanding of the biosynthesis and actions of neurosteroids in the brain neuron. This review also describes medicinal impact of neurosteroids on neurodegenerative disease.

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:558673 CAPLUS
DOCUMENT NUMBER: 141:168073
TITLE: 3α,5α-THP mediates progestins' effects to protect against adrenalectomy-induced cell death in the dentate gyrus of female and male rats
AUTHOR(S): Rhodes, Madeline E.; McCormick, Cheryl M.; Frye, Cheryl A.
CORPORATE SOURCE: Department of Psychology, Social Science 220, University at Albany-SUNY, Albany, NY, 12222, USA
SOURCE: Pharmacology, Biochemistry and Behavior (2004), 78(3), 505-512
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Progestins have neuroprotective effects in several in vitro models of neurodegeneration and in vivo in seizure models. The extent to which progesterone's in vivo protective effects may generalize to models not involving seizure processes and whether progesterone's protective effects are modulated by its metabolites have not been comprehensively investigated. The present expts. investigated the effects of progesterone and its metabolites, dihydryoprogesterone (DHP) and 5α-pregnan-3α-ol-20-one (3α,5α-THP), to protect the hippocampus from damage induced by adrenalectomy (ADX). In Expts. 1 and 2, progesterone, DHP, or 3α,5α-THP administration (1 mg/kg s.c.) to female (Experiment 1) or male (Experiment 2) rats similarly reduced the total number of ADX-induced pyknotic cells in the dentate gyrus compared with vehicle administration. In Experiment 3, blocking progesterone's metabolism to 3α,5α-THP with coadministration of a 5α-reductase inhibitor, finasteride (10 mg/kg s.c.), in female rats attenuated progesterone's protective effects on cell death in the dentate gyrus. Together, these data suggest that progestins can protect against ADX-induced cell death and that the actions of the progesterone metabolite, 3α,5α-THP, may underlie these effects.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:104154 CAPLUS
DOCUMENT NUMBER: 140:297748
TITLE: Reduced progesterone metabolites protect rat hippocampal neurones from kainic acid excitotoxicity in vivo
AUTHOR(S): Ciriza, I.; Azcoitia, I.; Garcia-Segura, L. M.
CORPORATE SOURCE: Instituto Cajal, CSIC, Madrid, Spain
SOURCE: Journal of Neuroendocrinology (2004), 16(1), 58-63

CODEN: JOUNE2; ISSN: 0953-8194
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ovarian hormone progesterone is neuroprotective in some animal models of neurodegeneration. Progesterone actions in the brain may partly be mediated by the locally produced metabolites 5α-dihydroprogesterone and 3α,5α-tetrahydroprogesterone. The neuroprotective effects of these two metabolites of progesterone were assessed in this study. Ovariectomized Wistar rats were injected with kainic acid, to induce excitotoxic neuronal death in the hippocampus, and with different doses of 5α-dihydroprogesterone and 3α,5α-tetrahydroprogesterone. The number of surviving neurons in the hilus of the dentate gyrus of the hippocampus was assessed with the optical disector method. The administration of kainic acid resulted in a significant decrease in the number of hilar neurons and in the induction of vimentin expression in reactive astrocytes, a sign of neural damage. Low doses of 5α-dihydroprogesterone (0.25 and 0.5 mg/kg body weight, b.w.) prevented the loss of hilar neurons and the appearance of vimentin immunoreactivity in astrocytes. Higher doses (1-2 mg/kg b.w.) were not neuroprotective. By contrast, low doses of 3α,5α-tetrahydroprogesterone (0.25-1 mg/kg b.w.) were unable to protect the hilus from kainic acid while higher doses (2-4 mg/kg b.w.) were protective. The different optimal neuroprotective doses of 5α-dihydroprogesterone and 3α,5α-tetrahydroprogesterone suggest that these two steroids may protect neurons using different mechanisms. The neuroprotective effects of 3α,5α-tetrahydroprogesterone may be exerted by the inhibition of neuronal activity via the GABAA receptor. This latter possibility is supported by the observation that 3β,5α-tetrahydroprogesterone, an isomer of 3α,5α-tetrahydroprogesterone that does not bind to GABAA receptor, was not neuroprotective. In summary, the authors' findings suggest that progesterone neuroprotective effects may be, at least in part, mediated by its reduced metabolites 5α-dihydroprogesterone and 3α,5α-tetrahydroprogesterone.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:293431 CAPLUS
DOCUMENT NUMBER: 136:304454
TITLE: Methods for the treatment of a traumatic central nervous system injury
INVENTOR(S): Stein, Donald Gerald; Hoffman, Stuart Wayne
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030409	A2	20020418	WO 2001-US31705	20011010

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,

GQ, GW, ML, MR, NE, SN, TD, TG

US 2002072509	A1	20020613	US 2001-973375		20011009
CA 2425650	AA	20020418	CA 2001-2425650		20011010
AU 2002011612	A5	20020422	AU 2002-11612		20011010
EP 1365752	A2	20031203	EP 2001-979677		20011010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004532796	T2	20041028	JP 2002-533852		20011010
US 2005187188	A1	20050825	US 2005-85889		20050322
PRIORITY APPLN. INFO.:			US 2000-239505P	P	20001011
			US 2000-245798P	P	20001103
			US 2001-973375	A	20011009
			WO 2001-US31705	W	20011010

AB The invention provides methods for conferring a neuroprotective effect on a population of cells in a subject following a traumatic injury to the central nervous system. Specifically, the methods of the invention provide for the administration of a progestin or progestin metabolite following a traumatic brain injury. The progestin or progestin metabolite is administered at therapeutically effective concns. that produce a neuroprotective effect (i.e., a decrease in the loss of neuronal activity) and reduces and/or prevents the various physiol. events leading to neurodegeneration, such as, cerebral edema and the immune/inflammatory response.

L8 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:547063 BIOSIS
DOCUMENT NUMBER: PREV200100547063
TITLE: Decreased neurosteroidogenesis in NP-C disease: Neuronal pathology and potential treatment.
AUTHOR(S): Griffin, L. D. [Reprint author]; Brown, C. L.; Mellon, S. H.
CORPORATE SOURCE: Neurology, UCSF, San Francisco, CA, USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 1205. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002

AB Niemann-Pick type C disease (NP-C) is a childhood neurodegenerative disease that is caused by mutations in the NPC1 protein, a lysosomal protein present in astrocytes. Lack of NPC1 protein results in cholesterol ester accumulation, and abnormal transport of cholesterol and other molecules within the cell. It is unclear how loss of NPC1 leads to neurodegeneration. Among the functions of cholesterol, it is used for neurosteroid synthesis. Our previous data that certain neurosteroids promote axonal and dendritic growth in neocortical neuronal cultures suggested that altered neurosteroidogenesis may result in abnormal neuronal development. We used a mouse model of NP-C to study the neurosteroid synthesis in different brain regions. Our data indicate that adult NP-C mouse brains contain much less of the neurosteroid pregnenolone than do normal Balb/c mice. At 9 wks, we detected region-specific decreases in P450scc, 5alphareductase, and 3alphaHSD activities. Brains from these mice synthesize 10% as much allopregnanolone as their age-matched littermate controls. Differences are also seen prior to symptom onset. There is gross neuronal loss throughout the brain; in the cerebellum, there is loss of virtually all Purkinje cells by 60d. P450scc, 3betaHSD, and 5alpha-reductase expression are significantly reduced in the regions in which they are normally expressed. Replacement of allopregnanolone to NP-C mice leads to partial amelioration

of the disease, coincident with enhanced neurosteroidogenic enzyme expression and cell survival. Our data suggest that decreased neurosteroidogenesis may contribute to the neuronal pathology, and that timed replacement of specific neurosteroids ameliorates this loss.

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ACCESSION NUMBER: 2004306972 EMBASE
TITLE: Brain on steroids resists neurodegeneration.
AUTHOR: Burns M.P.; Duff K.
CORPORATE SOURCE: M.P. Burns, Nathan Kline Institute, New York University, Orangeburg, NY 10962, United States
SOURCE: Nature Medicine, (2004) Vol. 10, No. 7, pp. 675-676. .
Refs: 9
ISSN: 1078-8956 CODEN: NAMEFI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Aug 2004
Last Updated on STN: 19 Aug 2004

AB A single injection of the neurosteroid allopregnanolone can delay the onset of neurological symptoms, decrease neuronal cell death and double the lifespan of mice with Niemann-Pick type C disease.

=> d L10 1-3 ibib abs

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:293431 CAPLUS
DOCUMENT NUMBER: 136:304454
TITLE: Methods for the treatment of a traumatic central nervous system injury
INVENTOR(S): Stein, Donald Gerald; Hoffman, Stuart Wayne
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030409	A2	20020418	WO 2001-US31705	20011010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002072509	A1	20020613	US 2001-973375	20011009
CA 2425650	AA	20020418	CA 2001-2425650	20011010
AU 2002011612	A5	20020422	AU 2002-11612	20011010
EP 1365752	A2	20031203	EP 2001-979677	20011010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004532796	T2	20041028	JP 2002-533852	20011010
US 2005187188	A1	20050825	US 2005-85889	20050322
PRIORITY APPLN. INFO.:			US 2000-239505P	P 20001011
			US 2000-245798P	P 20001103
			US 2001-973375	A 20011009
			WO 2001-US31705	W 20011010

AB The invention provides methods for conferring a neuroprotective effect on a population of cells in a subject following a traumatic injury to the central nervous system. Specifically, the methods of the invention provide for the administration of a progestin or progestin metabolite following a traumatic brain injury. The progestin or progestin metabolite is administered at therapeutically effective concns. that produce a neuroprotective effect (i.e., a decrease in the loss of neuronal activity) and reduces and/or prevents the various physiol. events leading to neurodegeneration, such as, cerebral edema and the immune/inflammatory response.

L10 ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005424746 EMBASE
TITLE: The case for progesterone.
AUTHOR: Stein D.G.
CORPORATE SOURCE: Dr. D.G. Stein, Department of Emergency Medicine, Emory University School of Medicine, Evans Bldg., 1648 Pierce Dr., NE, Atlanta, GA 30322, United States. dstei04@emory.edu
SOURCE: Annals of the New York Academy of Sciences, (2005) Vol. 1052, pp. 152-169. .
Refs: 89
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Oct 2005
Last Updated on STN: 20 Oct 2005

AB Recent clinical trials in hormone therapy (HT) for women approaching or past menopause have been disappointing. Most women who have been taking conjugated equine estrogens combined with synthetic progestins have been encouraged to stop these supplements because of increased health risks. The results of the clinical trials may be accurate about the risks associated with the synthetic compounds and combinations, but the data do not reflect what might have been the case if 17aβ-estradiol had been tested with natural progesterone instead of synthetic medrosyprogesterone acetate. For the most part, in almost all work on HT, estrogens have been given the primary focus despite the fact that progesterone has important properties that can enhance the repair of nenrodegenerative and traumatic injuries to the central nervous system. This article reviews some of those properties and discusses the evidence suggesting that, if HT is to be reconsidered, progesterone should be given more attention as a potent neurotrophic agent that may play an important role in reducing or preventing motor, cognitive, and sensory impairments that can accompany senescence in both males and females. .COPYRGT. 2005 New York Academy of Sciences.

L10 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003216234 EMBASE
TITLE: Estrogen and progesterone as neuroprotective agents in the treatment of acute brain injuries.

AUTHOR: Stein D.G.; Hoffman S.W.
CORPORATE SOURCE: D.G. Stein, Emory University, Department of Emergency Medicine, 1648 Pierce Drive, Atlanta, GA 30322, United States. dstei04@emory.edu
SOURCE: Pediatric Rehabilitation, (2003) Vol. 6, No. 1, pp. 13-22.
.
Refs: 91
ISSN: 1363-8491 CODEN: PEREFP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jun 2003
Last Updated on STN: 12 Jun 2003

AB Estrogen and progesterone are often thought of as steroid hormones that strongly influence reproductive and maternal behaviours. However, the steroids are now showing considerable promise as neuroprotective and neuroregenerative agents in stroke and traumatic brain injuries. Collectively, these two hormones have been reported to reduce the consequences of the injury cascade by enhancing anti-oxidant mechanisms, reducing excitotoxicity: altering glutamate receptor activity, reducing immune inflammation, providing neurotrophic support, stimulating axonal remyelinization and enhancing synaptogenesis and dendritic arborization. Estrogen has often been tried as a prophylactic treatment in females for ischemic brain injury, while progesterone has, thus far, been given as a post-injury treatment for both male and female subjects with acute, ischemic and traumatic injuries of the brain and spinal cord. This review compares and evaluates estrogen and progesterone as neuroactive agents in the acute treatment of brain damage caused by stroke and trauma.

```
=> s central nervous system
L11     769760 CENTRAL NERVOUS SYSTEM

=> s L6 and L11
L12        156 L6 AND L11

=> s L12 and (AY<2002 or PY<2002 or PRY<2002)
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
   2 FILES SEARCHED...
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
L13         94 L12 AND (AY<2002 OR PY<2002 OR PRY<2002)

=> s central nervous system injury
L14       2105 CENTRAL NERVOUS SYSTEM INJURY

=> s L6 and L14
L15          1 L6 AND L14

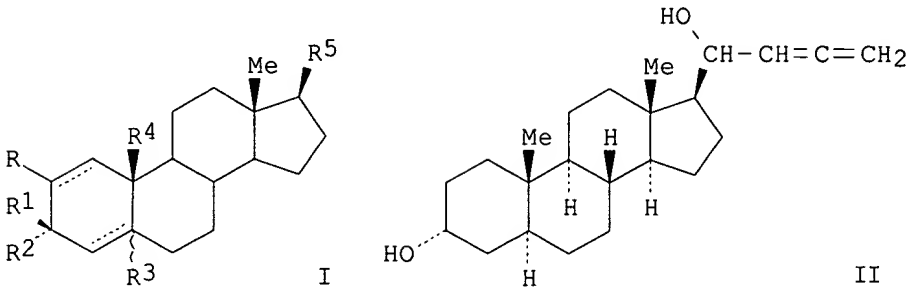
=> d L13 1-10 ibib abs

L13  ANSWER 1 OF 94  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:12134  CAPLUS
DOCUMENT NUMBER:         142:56565
TITLE:                   Preparation of steroids as GABAA modulating
                         neurosteroids
```

INVENTOR(S): Kalogeropoulou, Theodora; Makrygiannis, Alexandros; Souli, Charikleia; Tsotinis, Andreas
PATENT ASSIGNEE(S): Greece
SOURCE: Greek, 33 pp.
CODEN: GRXXCX
DOCUMENT TYPE: Patent
LANGUAGE: Greek
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
GR 1003861	B1	20020411	GR 2000-100470		20001229	<--
AU 2002217353	A1	20020716	AU 2002-217353		20011221	<--
US 2005176976	A1	20050811	US 2002-250334		20011221	<--
US 7064116	B2	20060620	US 2003-250334		20030630	<--
PRIORITY APPLN. INFO.:			GR 2000-100470	A	20001229	<--
			WO 2001-GR48	W	20011221	<--

OTHER SOURCE(S): MARPAT 142:56565
GI



AB Steroid derivs. of formula I [R, R1 = H, etc.; R2 = OH, NCS, etc.; R3 = H, absent; R4 = H, alkyl, etc.; R5 = hydroxyalkyl, alkoxyalkyl, (substituted) C.tplbond.CH, COCH2N3, COCH2Br, COMe, etc.] are prepared that act on the γ-aminobutyric acid receptor-chloride ionophore (GR) complex and their applications to induce anesthesia, in the treatment of stress, anxiety, PMS, PND, and seizures such as those caused by epilepsy, to ameliorate or prevent the attacks of anxiety, muscle tension, and depression common with patients suffering from central nervous system abnormalities. The present invention also includes formulations which consist of one or more of the compds. of formula I. Thus, II was prepared and hac EC50 of 5.9 nM against GABAA receptor.

L13 ANSWER 2 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:428567 CAPLUS
DOCUMENT NUMBER: 140:400098
TITLE: Neurosteroid regulation-based method of screening for nonsteroidal neuropsychiatric agents
INVENTOR(S): Davis, John M.; Uzunov, Doncho P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6740500 B1 20040525 US 2000-534831 20000323 <--
PRIORITY APPLN. INFO.: US 2000-534831 20000323 <--

AB A method of screening for nonsteroidal neuropsychiatric agents includes determining the ability of a candidate nonsteroidal agent to selectively regulate or alter the central nervous system content and/or bioavailability of an endogenous neuroactive steroid. In particular, the method includes determining the ability of the agent to selectively regulate a rate-limiting step in the biocontrol of the bioavailable amount of an endogenous neuroactive steroid, wherein the rate-limiting step may be either a step in biosynthesis of an endogenous neuroactive steroid, e.g. allopregnanolone, or a step in the biodegrdn. of such an endogenous neuroactive steroid. Alternatively, the method may include determining the ability of a candidate agent in selectively regulating the rate of reuptake of an endogenous neuroactive steroid by neurons or glial cells.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:570823 CAPLUS
DOCUMENT NUMBER: 139:112167
TITLE: Pregnane steroids for use in the treatment of steroid-related CNS disorders
INVENTOR(S): Baeckstroem, Torbjoern; Lundgren, Per; Wang, Ming-de; Johansson, Inga-maj
PATENT ASSIGNEE(S): Umecrine Ab, Swed.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059357	A1	20030724	WO 2002-SE2423	20021220 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2468248	AA	20030724	CA 2002-2468248	20021220 <--
AU 2002359202	A1	20030730	AU 2002-359202	20021220 <--
EP 1458399	A1	20040922	EP 2002-793723	20021220 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1607954	A	20050420	CN 2002-826275	20021220 <--
JP 2005519893	T2	20050707	JP 2003-559519	20021220 <--
US 2005222099	A1	20051006	US 2005-499214	20050428 <--
PRIORITY APPLN. INFO.:			SE 2001-4423 A	20011227 <--
			WO 2002-SE2423 W	20021220

AB Steroid compds. possessing a hydrogen donor in 3β position, either in the form of a hydroxy- or a sulfate group, function as efficient blockers of the 3α-hydroxy-pregnane-steroid action and thus have utility as therapeutic substances for the prevention and/or treatment of steroid related CNS disorders. Treatment methods based on the administration of these substances are disclosed, and these substances either alone or in combination are also suggested for the manufacture of pharmaceuticals for the treatment of many specific steroid induced CNS disorders.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:173815 CAPLUS
DOCUMENT NUMBER: 138:217464
TITLE: Crystal structure of human 3α-hydroxysteroid dehydrogenase and its use to identify modulators
INVENTOR(S): Floersheim, Philipp; Ostermeier, Christian; Uzunov, Doncho; Jahnke, Wolfgang
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003018830	A2	20030306	WO 2002-EP9366		20020821 <--
WO 2003018830	A3	20031113			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW					
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR					
EP 1421383	A2	20040526	EP 2002-796261		20020821 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005500853	T2	20050113	JP 2003-523677		20020821 <--
US 2005202505	A1	20050915	US 2004-486660		20040212 <--
PRIORITY APPLN. INFO.:			US 2001-314045P	P	20010822 <--
			WO 2002-EP9366	W	20020821

AB 3α-Hydroxysteroid dehydrogenase (I) plays a central role in the metabolism and action of steroid hormones and neurosteroids (steroids synthesized in the central nervous system).
The high-resolution structure of human I crystallized in complex with cofactor NADP is determined by x-ray diffraction. The crystals have rhombohedral space group symmetry and a unit cell with dimensions a = b = c = 108.5 Å, α = β = γ = 85.1°. The enzyme core is formed by an α/β barrel with a cylindrical core of eight parallel β-strands surrounded by eight α-helixes which run anti-parallel to the β-sheet. This barrel is formed by repeating the β/α unit eight times with two deviations: (1) an addnl. helix exists between β-strand 7 and helix 8 of the barrel; and (2) a second helix exists between helix 8 and the C-terminal region. Furthermore, the 3-dimensional structure of active site and cofactor-binding site is determined The structure coordinates of the enzyme may be used to design and select novel classes of modulators to human I. Rational drug design, NMR screening methods, in silico Gold Docking, mol. replacement, and in vitro functional assays are provided to identify inhibitors of I.

L13 ANSWER 5 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:730545 CAPLUS
DOCUMENT NUMBER: 137:242465
TITLE: Method and compounds for use in the treatment of steroid induced states of the central nervous system
INVENTOR(S): Backstrom, Torbjorn; Wang, Ming-De
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 37,869,

abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

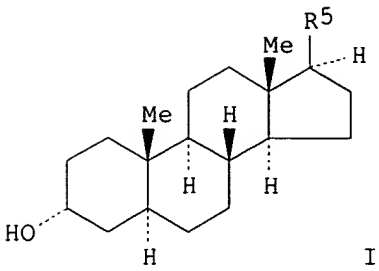
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6455516	B1	20020924	US 1999-266035	19990311 <--
PRIORITY APPLN. INFO.:			US 1998-37869 B2	19980311 <--

OTHER SOURCE(S): MARPAT 137:242465
AB The use of epiallopregnanolone (3β-hydroxy-5α-pregnan-20-one) for the treatment of steroid induced mood disorders and CNS disorders is disclosed. Further, the use of epiallopregnanolone for the manufacture of pharmaceuticals is disclosed, together with an list of symptoms suitable for treatment with epiallopregnanolone.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:521760 CAPLUS
DOCUMENT NUMBER: 137:79112
TITLE: Preparation of GABAA modulating neurosteroids for therapeutic use in the treatment of central nervous system abnormalities
INVENTOR(S): Calogeropoulou, Theodora; Tsotinis, Andrew; Souli, Charikleia; Makriyannis, Alexandros
PATENT ASSIGNEE(S): Elpen S.A., Greece
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053577	A2	20020711	WO 2001-GR48	20011221 <--
WO 2002053577	A3	20021010		
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TN, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2002217353	A1	20020716	AU 2002-217353	20011221 <--
US 2005176976	A1	20050811	US 2002-250334	20011221 <--
US 7064116	B2	20060620	US 2003-250334	20030630 <--
PRIORITY APPLN. INFO.:			GR 2000-10047 A	20001229 <--
			GR 2000-100470 A	20001229 <--
			WO 2001-GR48 W	20011221 <--

OTHER SOURCE(S): MARPAT 137:79112
GI



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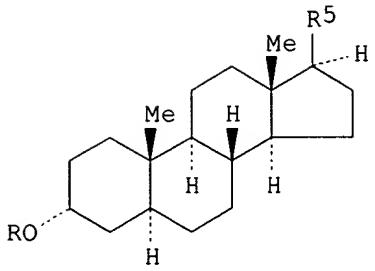

II

AB Novel steroid derivs., such as I [R5 = CH(OR6)R7, C.tplbond.C-aryl, C.tplbond.CCH(OR6)R7, C.tplbond.CCOR8, COCH2N3, COCH2Br, COMe, etc.; R6 = H, alkyl, alkenyl, alkynyl; R7 = allene, alkynyl, etc.; R8 = H, alkyl, alkenyl, arylalkyl, aryl], were prepared for use as γ-aminobutyric acid receptor (GABAA) agonists for pharmaceutical use in the treatment of patients suffering from central nervous system abnormalities, such as stress, anxiety, PMS, PND, and seizures such as those caused by epilepsy, to ameliorate or prevent the attacks of anxiety, muscle tension, and depression, and to induce anesthesia. Thus, silylated carboxaldehyde II (R = SiPh2CMe3, R5 = CHO) was reacted with CBr4 using Ph3Ph in CH2Cl2 to give II (R = SiPh2CMe3, R5 = CH:CBr2) in 93% yield which was, in turn, treated with TBAF in THF to give II (R = H, R5 = C.tplbond.CBr) in 70% yield. The prepared neurosteroids were assayed for their ability to enhance the binding of [3H]-Flunitrazepam to the benzodiazepinesite in rat brain GBR enriched synaptosomal preparation

L13 ANSWER 7 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:293431 CAPLUS
DOCUMENT NUMBER: 136:304454
TITLE: Methods for the treatment of a traumatic central nervous system injury
INVENTOR(S): Stein, Donald Gerald; Hoffman, Stuart Wayne
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030409	A2	20020418	WO 2001-US31705	20011010 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002072509	A1	20020613	US 2001-973375	20011009 <--
CA 2425650	AA	20020418	CA 2001-2425650	20011010 <--
AU 2002011612	A5	20020422	AU 2002-11612	20011010 <--
EP 1365752	A2	20031203	EP 2001-979677	20011010 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532796	T2	20041028	JP 2002-533852	20011010 <--

US 2005187188 A1 20050825 US 2005-85889 20050322 <--
PRIORITY APPLN. INFO.: US 2000-239505P P 20001011 <--
US 2000-245798P P 20001103 <--
US 2001-973375 A 20011009 <--
WO 2001-US31705 W 20011010 <--

AB The invention provides methods for conferring a neuroprotective effect on a population of cells in a subject following a traumatic injury to the central nervous system. Specifically, the methods of the invention provide for the administration of a progestin or progestin metabolite following a traumatic brain injury. The progestin or progestin metabolite is administered at therapeutically effective concns. that produce a neuroprotective effect (i.e., a decrease in the loss of neuronal activity) and reduces and/or prevents the various physiol. events leading to neurodegeneration, such as, cerebral edema and the immune/inflammatory response.

L13 ANSWER 8 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:127978 CAPLUS
DOCUMENT NUMBER: 137:77134
TITLE: Circulating levels of allopregnanolone, an anticonvulsant metabolite of progesterone, in women with partial epilepsy in the postcritical phase
AUTHOR(S): Galli, Renato; Luisi, Michele; Pizzanelli, Chiara; Monteleone, Patrizia; Casarosa, Elena; Iudice, Alfonso; Murri, Luigi
CORPORATE SOURCE: Department of Neuroscience, Section of Neurology, Endocrine Research Unit, C.N.R., University of Pisa, Pisa, Italy
SOURCE: Epilepsia (2001), 42(2), 216-219
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Several lines of evidence indicate that there exists a relation between ovarian hormones and epilepsy. Estrogens decrease seizure threshold and increase brain excitability, whereas progesterone has an inhibitory effect and reduces epileptiform activity. Recently considerable interest has turned to neuroactive steroids, a group of progesterone metabolites, as endogenous modulators of excitability of the central nervous system (CNS). Their ability to alter neuronal firing rapidly occurs through interaction with γ-aminobutyric acid (GABA) A receptor complex. In a previous experience, serum allopregnanolone (3α-OH-5α-pregnan-20-one) levels were measured in 15 women with partial epilepsy in the intercrit. phase, and no significant differences were found between patients and control subjects. Methods: To find out if there are changes in serum allopregnanolone levels after epileptic seizure, blood samples were drawn immediately, 15 min, and 6 h after a seizure in 7 fertile females with partial epilepsy. Results: The most interesting finding is that allopregnanolone increases in serum during the first 15 min after partial seizures ($p < 0.05$) and decreases after 6 h. Conclusions: These data are consistent with a role for allopregnanolone in the control of neuronal excitability and seizures.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:770695 CAPLUS
DOCUMENT NUMBER: 136:48525
TITLE: Stress and neuroactive steroids
AUTHOR(S): Barbaccia, Maria Luisa; Serra, Mariangela; Purdy, Robert H.; Biggio, Giovanni
CORPORATE SOURCE: Department of Neuroscience, University of Rome "Tor

Vergata", Rome, 00133, Italy
SOURCE: International Review of Neurobiology (2001), 46(Neurosteroids and Brain Function), 243-272
CODEN: IRNEAE; ISSN: 0074-7742
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with .apprx.120 refs. The discovery that the endogenous steroid derivs. 3α-hydroxy-5α-pregnan-20-one (allopregnanolone , or 3α,5α-TH PROG) and 3α,21-dihydroxy-5α-pregnan-20-one (allotetrahydrodeoxycorticosterone, or 3α, 5α-TH DOC) elicit marked anxiolytic and anti-stress effects and selectively facilitate GABA-mediated neurotransmission in the central nervous system has provided new perspectives for our understanding of the physiol. and neurobiol. of stress and anxiety. Evidence indicating that various stressful conditions that downregulate GABAergic transmission and induce anxiety-like states also induce marked increases in the plasma and brain concns. of these neuroactive steroids has led to the view that stress, neurosteroids, and the function of GABAA receptors are intimately related. Changes in the brain concns. of neurosteroids may play an important role in the modulation of emotional state as well as in the homeostatic mechanisms that counteract the neuronal overexcitation elicited by acute stress. Indeed, neurosteroids not only interact directly with GABAA receptors but also regulate the expression of genes that encode subunits of this receptor complex. This chapter summarizes observations from our labs. and others, suggesting that neurosteroids and GABAergic transmission are important contributors to the changes in emotional state induced by environmental stress. (c) 2001 Academic Press.
REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:729336 CAPLUS
DOCUMENT NUMBER: 136:31764
TITLE: Pre-menstrual steroids
AUTHOR(S): Smith, S. S.
CORPORATE SOURCE: Department of Physiology and Pharmacology, SUNY Health Science Center at Brooklyn, Brooklyn, NY, 11203, USA
SOURCE: Cellular and Molecular Life Sciences (2001), 58(9), 1263-1275
CODEN: CMLSFI; ISSN: 1420-682X
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 123 refs. A number of steroid hormones and their metabolites fluctuate in the circulation across the human menstrual cycle. In addition to their classic actions on the hypothalamo-pituitary-gonadal axis, many of these hormones act as neuroactive steroids to alter the function of neurotransmitters, such as GABA, within central nervous system circuits. Clin., these steroids are important because they have not only acute but also long-term effects, and withdrawal properties. This review discusses the effects of steroids such as 3α-OH-5α-pregnan-20-one (3α,5α-THP or allopregnanolone) which alter GABA function in distinct ways dependent upon the time course of exposure, to either enhance or decrease inhibition in the brain. These effects are discussed in light of recent clin. findings which seek to further characterize the steroid milieu which underlies pre-menstrual dysphoria.
REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 11-25 ibib abs L13

L13 ANSWER 11 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:620725 CAPLUS
DOCUMENT NUMBER: 135:252183
TITLE: Effects of CRH and ACTH administration on plasma and brain neurosteroid levels
AUTHOR(S): Torres, J. M.; Ruiz, E.; Ortega, E.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Granada, Granada, 18012, Spain
SOURCE: Neurochemical Research (2001), 26(5), 555-558
CODEN: NEREDZ; ISSN: 0364-3190
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 3α-hydroxy ring A-reduced metabolite of progesterone, 3α-hydroxy-5α-pregnan-20-one (allopregnanolone) is among the most potent known ligands of the gamma aminobutyric acid (GABA) receptor, designated GABA-A, in the central nervous system. The authors determined by RIA serum levels of progesterone (PROG), 5-α-dihydroprogesterone (DHP) and allopregnanolone in male and female rats after corticotropin releasing hormone (CRH) and ACTH hormone (ACTH) administration. Allopregnanolone was undetectable in plasma and brain of control males but detectable in plasma and brain of males injected with CRH and ACTH and of control and similarly treated females. Allopregnanolone increased in the plasma and brain after CRH and ACTH administration in all cases. The data demonstrate that the administration of CRH plus ACTH results in a rapid increase of the neuroactive steroid allopregnanolone in the brain of males and females to levels known to modulate GABA-A receptor function. Thus, stress could regulate neurosteroid biosynthesis via the hormones ACTH and CRH.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:399111 CAPLUS
DOCUMENT NUMBER: 135:221185
TITLE: Sensitivity of synaptic GABAA receptors to allosteric modulators in hippocampal oriens-alveus interneurons
AUTHOR(S): Patenaude, Christian; Nurse, Suzanne; Lacaille, Jean-Claude
CORPORATE SOURCE: Centre de recherche en sciences neurologiques and Departement de physiologie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.
SOURCE: Synapse (New York, NY, United States) (2001), 41(1), 29-39
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GABAA receptors are heteropentamers that are heterogeneously distributed at different synapses in the central nervous system. Although the modulation of GABAA receptors received much attention in hippocampal pyramidal cells, information is scarce regarding the pharmacol. of these receptors in inhibitory interneurons. The authors investigated the pharmacol. properties of GABAA-mediated miniature inhibitory postsynaptic currents (mIPSCs) using whole-cell voltage clamp recordings in two morphol. identified types of hippocampal CA1 interneurons, horizontal and vertical cells of stratum oriens-alveus. The neg. modulators zinc (200 μM) and furosemide (600 μM) significantly

decreased the amplitude of mIPSCs. Benzodiazepine agonists also produced significant effects: 10 μM zolpidem increased the amplitude, rise time, and decay time constant (decay τ) of mIPSCs, whereas 10 μM flunitrazepam affected similarly the amplitude and decay τ, but not the rise time. The neurosteroid allopregnanolone (10 μM) prolonged the decay τ of mIPSCs. Since these modulators act on different GABAA receptor subunits, this pharmacol. profile suggests that GABAA receptors at spontaneously active inhibitory synapses onto vertical and horizontal interneurons are heterogeneous and formed by coassembly of different combinations of subunits (α1-5β1-3γ1-3). Furthermore, these synaptic GABAA receptors appear in large part pharmacol. similar to those of pyramidal cells.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:166927 CAPLUS
DOCUMENT NUMBER: 134:276723
TITLE: Development of antidotes for sodium monofluoroacetate (1080)
AUTHOR(S): Cook, Christian J.; Eason, Charles T.; Wickstrom, Mark; Devine, Chris D.
CORPORATE SOURCE: Technology Development Group, HortResearch, Hamilton, N. Z.
SOURCE: Biomarkers (2001), 6(1), 72-76
CODEN: BIOMFA; ISSN: 1354-750X
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Baits containing Na monofluoroacetate (1080) are commonly used in New Zealand during feral pest control operations. However, each year, a number of domestic dogs are unintentionally killed during these control operations, and a suitable antidote to 1080 intoxication is required. The primary toxic mechanism of 1080 is well known. However, as with other pathologies where energy deprivation is the main effect of intoxication, the cascade of effects that arises from this primary mechanism is complex. At present, putative antidotes for 1080 are generally unable to address the primary mechanism of intoxication but such agents may be able to control the cascade of secondary effects, which can result during intoxication. Part of the reason for this is that targeting the cascade can provide a longer window of time for antidote success. We have undertaken studies that identified some of the central nervous system (CNS) and systemic pathophysiol. cascades caused by 1080 intoxication. Using this information we designed antidotes, on the basis of preventing different steps in this cascade. In the chicken model targeting systemic changes, in particular reducing effects of nitric oxide derivs. generated in cardiac muscle, proved successful in reducing fatality associated with 1080. In rats and sheep, targeting the CNS with a number of compds. including: glutamate; calcium and dopamine antagonists; gamma amino butyric acid agonists, and astressin-like compds. reduced fatalities. However, to be successful in the rat and sheep model a given antidote needed to move quickly from systemic circulation across the blood brain barrier and into the CNS. The work also suggests ways in which specific biomarkers of 1080 exposure may be developed with respect to different species.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:93238 CAPLUS
DOCUMENT NUMBER: 134:141992
TITLE: Acute neuroactive steroid withdrawal in withdrawal seizure-prone and withdrawal seizure-resistant mice
AUTHOR(S): Reilly, M. T.; Crabbe, J. C.; Rustay, N. R.; Finn, D.

A.
CORPORATE SOURCE: Portland Alcohol Research Center, Department of Behavioral Neuroscience, Oregon Health Sciences University, Portland, OR, 97201, USA
SOURCE: Pharmacology, Biochemistry and Behavior (2000), 67(4), 709-717
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Allopregnanolone (3α-hydroxy-5α-pregnan-20-one) is an endogenously derived metabolite of progesterone, and a potent pos. modulator of GABAA receptors. A withdrawal syndrome, characterized by central nervous system (CNS) hyperexcitability, has been demonstrated following abrupt discontinuation of high progesterone levels in rats, which was due in part to altered levels of allopregnanolone. The purpose of the present study was to determine if a single administration of pregnanolone or allopregnanolone could produce an acute withdrawal response in mice selected for susceptibility (Withdrawal Seizure-Prone, WSP) or resistance (Withdrawal Seizure-Resistant, WSR) to ethanol withdrawal convulsions. WSP mice administered 75 mg/kg pregnanolone showed a significant increase in handling-induced convulsion (HIC) scores over a 25-h testing period. In contrast, HIC scores in WSR mice were negligible after acute administration of 25, 50, 75, or 100 mg/kg pregnanolone. WSP mice also showed a similar increase in HIC after withdrawal from 75 mg/kg allopregnanolone. This effect was evident at both the 10-h and 25-h overall withdrawal severity assessment. These results demonstrate that neuroactive steroids can elicit an acute withdrawal response similar to that of other pos. modulators of GABAA receptors in WSP mice, supporting the notion that a common set of genes underlie acute and chronic withdrawal severity from multiple agents with depressant effects on the central nervous system.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:734451 CAPLUS
DOCUMENT NUMBER: 133:329799
TITLE: Effects of estradiol and raloxifene analog on brain, adrenal and serum allopregnanolone content in fertile and ovariectomized female rats
AUTHOR(S): Genazzani, Andrea R.; Bernardi, Francesca; Stomati, Massimo; Monteleone, Patrizia; Luisi, Stefano; Rubino, Silvia; Farzati, Angelo; Casarosa, Elena; Luisi, Michele; Petraglia, Felice
CORPORATE SOURCE: Department of Reproductive Medicine and Child Development, Division of Obstetrics and Gynecology, University of Pisa, Pisa, I-56100, Italy
SOURCE: Neuroendocrinology (2000), 72(3), 162-170
CODEN: NUNDAJ; ISSN: 0028-3835
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Allopregnanolone is a neuroactive steroid synthesized in rat gonads, adrenal cortex, and central nervous system. It has been suggested that sex steroid hormones might influence allopregnanolone concns. but no clear data have ever been reported. The aim of the present study was to investigate the effects of administration of 17β-estradiol (17β-E2), the raloxifene analog LY-117018 or their combination on allopregnanolone levels in fertile and ovariectomized (OVX) rats. Thirteen groups of 12 Wistar female rats each received either 17β-E2 (0.1 or 1 μg/day) or LY-117018 (25, 250, and 1250 μg/day), or

17β-E2 1 μg/day plus LY-117018: 25, 250, and 1250 μg/day for 14 days. The rats were then sacrificed and allopregnanolone content was assessed in the hypothalamus, hippocampus, pituitary, adrenals, and serum. Ovariectomy determined a significant decrease in allopregnanolone content in the hypothalamus, hippocampus, pituitary, and serum, while increasing it in the adrenals ($p < 0.01$). In OVX rats, the administration of either 17β-E2 or LY-117018 restored ovariectomy-induced allopregnanolone changes. The administration of LY-117018 in addition to 17β-E2 to OVX animals suppressed the increase in allopregnanolone levels determined by 17β-E2 in the hippocampus, hypothalamus, and pituitary, but not in the adrenals and serum. In fertile rats, the administration of LY-117018 reproduced the effects of ovariectomy. This study shows that the raloxifene analog LY-117018 has an estrogen-like action on the central nervous system of OVX rats when administered alone, while it acts as an antiestrogen in the presence of 17β-E2, both in OVX animals treated with 17β-E2 and in fertile rats. A different effect was observed in the adrenal glands. The mechanism of action of this compound has still to be clarified.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:587842 CAPLUS

DOCUMENT NUMBER: 133:291177

TITLE: Progesterone, progestagens and the central nervous system

AUTHOR(S): Genazzani, A. R.; Stomati, M.; Morittu, A.; Bernardi, F.; Monteleone, P.; Casarosa, E.; Gallo, R.; Salvestroni, C.; Luisi, M.

CORPORATE SOURCE: Department of Reproductive Medicine and Child Development, Division of Gynecology and Obstetrics, University of Pisa, Pisa, 56100, Italy

SOURCE: Human Reproduction (2000), 15(Suppl. 1), 14-27
CODEN: HUREEE; ISSN: 0268-1161

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 57 refs.,. Estrogen, progestagens and androgens are able to modulate several brain functions. Receptors for gonadal steroids have been identified in several brain areas: amygdala, hippocampus, cortex, basal forebrain, cerebellum, locus ceruleus, midbrain rafe nuclei, glial cells, pituitary gland, hypothalamus and central gray matter. The mechanism of action of sex steroids at this level is similar to that observed in the peripheral target organs, including both genomic and non-genomic effects. The increased use of sex steroid hormone derivative therapies has lead to study of the biochem. and metabolic properties of the different progestin mols. available in hormonal therapies. In particular, exptl. and clin. studies focused the attention of researchers on interactions between estrogens and progestins in the neuroendocrine control of the brain functions and its clin. implications. Moreover, steroids are also synthesized de novo in the brain or may be derived from the conversion of blood-borne precursors, suggesting that the brain is also a source of steroids, named neurosteroids. Neurosteroids exert non-classical rapid actions as allosteric agonists of γ-aminobutyric acid receptor A (GABAA) and also modulate classic neurotransmitters in the brain. In addition, progesterone derivs., e.g., pregnanolone, and 3α 5α-OH THP (allopregnanolone) are synthesized de novo by astrocytes and oligodendrocites starting from cholesterol. Physiol. or pathol. modifications of the synthesis and release of neurosteroids play a relevant role in the control of brain function.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:521450 CAPLUS
DOCUMENT NUMBER: 133:188139
TITLE: Serum allopregnanolone levels in pregnant women: changes during pregnancy, at delivery, and in hypertensive patients
AUTHOR(S): Luisi, S.; Petraglia, F.; Benedetto, C.; Nappi, R. E.; Bernardi, F.; Fadalti, M.; Reis, F. M.; Luisi, M.; Genazzani, A. R.
CORPORATE SOURCE: Department of Reproductive Medicine and Child Development, Section of Gynecology and Obstetrics, University of Pisa, Pisa, Italy
SOURCE: Journal of Clinical Endocrinology and Metabolism (2000), 85(7), 2429-2433
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Allopregnanolone is a neuroactive steroid measurable in peripheral circulation. The aim of the present study was to investigate the presence and the possible changes in serum allopregnanolone and progesterone levels in pregnant women during gestation, at delivery, and in patients with chronic hypertension, with or without superimposed preeclampsia. We also evaluated allopregnanolone in cord blood. Three groups of pregnant women were studied: (1) healthy controls followed longitudinally throughout gestation (n = 14); (2) at vaginal or cesarean delivery (n = 66); and (3) with chronic hypertension (n = 12), with (n = 7) or without (n = 5) superimposed preeclampsia. Allopregnanolone and progesterone levels were measured in maternal and cord serum by RIA. In healthy pregnant women, serum allopregnanolone and progesterone levels progressively increased throughout gestation. Whereas no changes were found at vaginal delivery, serum allopregnanolone and progesterone levels were significantly lower at delivery by emergency cesarean section ($P < 0.01$). Umbilical cord serum allopregnanolone and progesterone levels in emergency cesarean were significantly lower than those found at vaginal delivery ($P < 0.01$). Patients with chronic hypertension, with or without superimposed severe preeclampsia, showed serum allopregnanolone levels significantly higher than those of healthy women at the same gestational age ($P < 0.01$). In conclusion, maternal serum allopregnanolone levels increased during normal gestation were lower in women who underwent emergency cesarean and higher in patients with chronic hypertension, with or without preeclampsia. Because allopregnanolone is active on the central nervous system and in the control of systemic blood pressure, an involvement of this neurosteroid in the adaptive processes induced by pregnancy is suggested.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:398255 CAPLUS
DOCUMENT NUMBER: 133:115018
TITLE: Comparison of the neurophysiological effects of allopregnanolone and ethanol in rats
AUTHOR(S): Slawecki, C. J.; Walpole, T.; Purdy, R. H.; Ehlers, C. L.
CORPORATE SOURCE: Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Psychopharmacology (Berlin) (2000), 149(4), 351-359
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rationale: The central nervous system actions of allopregnanolone (3α-hydroxy-5α-pregnan-20-one) and ethanol are at least partially mediated by modulation of γ-aminobutyric acid (GABA)-A receptors. Although ethanol and allopregnanolone have similar behavioral effects, their macro-electrophysiol. profiles have not been directly compared. Objective: The purpose of this study was to compare the effects of allopregnanolone and ethanol on the EEG (EEG) and event-related potentials (ERPs). Methods: Male Wistar rats were implanted with cortical and amygdalar electrodes. The rats were then administered allopregnanolone (0.0-10 mg/kg), ethanol (0.0-1.0 g/kg), or a combination of the two before recording. Results: Allopregnanolone and ethanol had similar effects on ERPs. When administered alone, both decreased cortical P1-N1 ERP amplitude by 25-50% and N1 amplitude in the amygdala by 75-80%. Combined administration of ethanol (0.50 g/kg) and allopregnanolone (5.0 mg/kg), doses which were ineffective alone, decreased N1 amplitude in the amygdala by 60%. Allopregnanolone and ethanol had dissimilar EEG effects. Allopregnanolone increased high frequency power in the cortex and amygdala by 25-30%. Ethanol decreased cortical and amygdalar power in the same high frequency bands by 25-45%. Allopregnanolone, but not ethanol, also shifted cortical frequency in the 32- to 50-Hz band. Combined administration of allopregnanolone and ethanol had no effect on EEG power but enhanced allopregnanolone's effect on cortical frequency. Conclusions: These data suggest that allopregnanolone's macro-electrophysiol. profile resembles barbiturates and benzodiazepines more than ethanol. Further, the interactions of allopregnanolone and ethanol appear complex, with multiple effects observed (enhancement or reversal) depending on the neurophysiol. variable assessed.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 19 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:395968 CAPLUS

DOCUMENT NUMBER: 133:188346

TITLE: Characterisation of GABAA receptors in fetal, neonatal and adult ovine brain: region and age related changes and the effects of allopregnanolone

AUTHOR(S): Crossley, K. J.; Walker, D. W.; Beart, P. M.; Hirst, J. J.

CORPORATE SOURCE: Department of Physiology, Monash University, Clayton, 3168, Australia

SOURCE: Neuropharmacology (2000), 39(9), 1514-1522
CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Progesterone metabolites acting via GABAA receptors suppress central nervous system (CNS) activity. The aim of the present study was to examine binding characteristics of GABAA receptors in fetal, newborn and adult sheep brains using [35S]TBPS, and to determine the effects of allopregnanolone on this binding. Receptor affinity (KD) and d.. (BMAX) in the brainstem were not different in fetal, newborn (1-2 days old) and adult brains. In the hypothalamus KD and BMAX increased significantly in the fetus between 85 and 128 days gestation, and were then similar to postnatal and adult values. In the frontal cortex KD and BMAX increased progressively between 85 days and term (.apprx.147 days gestation), and were then not different from postnatal and adult values. The Ki values for the GABAA receptor antagonist picrotoxin was similar at all ages. Allopregnanolone inhibited [35S]TBPS binding in the presence of 5 μM GABA, but enhanced binding in the absence of GABA. These results show that (i), functional GABAA

receptors are present in the fetal brain from at least 85 days gestation; (ii), 3α-pregnane steroids modify receptor affinity in the late gestation fetal brain; and (iii) there are region-specific changes in GABAA receptor binding parameters. Steroid modulation of the GABAA receptor in the fetal brain is likely to influence fetal CNS activity in late gestation.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 20 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:193022 CAPLUS
DOCUMENT NUMBER: 132:288956
TITLE: The neurosteroid allopregnanolone modulates oxytocin expression in the hypothalamic paraventricular nucleus
AUTHOR(S): Blyth, Brian J.; Hauger, Richard L.; Purdy, Robert H.; Amico, Janet A.
CORPORATE SOURCE: Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15261, USA
SOURCE: American Journal of Physiology (2000), 278(3, Pt. 2), R684-R691
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Virgin, ovariectomized rats exposed to 2 wk of sequential estradiol (E2) and progesterone (P) followed by P withdrawal have increased hypothalamic oxytocin (OT) mRNA and peptide levels relative to sham-treated animals. This increase is prevented if P is sustained. In the central nervous system, P is metabolized to the neurosteroid allopregnanolone (3α-hydroxy-5α-pregnan-20-one), which exerts effects by acting as a pos. allosteric modulator of GABAA receptor/Cl--channel complexes. In the present study, ovariectomized rats that received sequential E2 and P for 2 wk followed by P withdrawal were administered allopregnanolone at the time of P withdrawal. Hypothalamic and plasma allopregnanolone concns., serum E2 and P concns., and hypothalamic OT mRNA levels were measured at death. Steroid-induced increases in OT mRNA were attenuated in animals treated with allopregnanolone at the time of P withdrawal. The results suggest that allopregnanolone plays an important modulatory role in steroid-mediated increases in hypothalamic OT.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:189613 CAPLUS
DOCUMENT NUMBER: 132:303629
TITLE: In vivo evidences of early neurosteroid synthesis in the developing rat central nervous system and placenta
AUTHOR(S): Pomata, P. E.; Colman-Lerner, A. A.; Baranao, J. L.; Fiszman, M. L.
CORPORATE SOURCE: Laboratorio de Neurociencias, Centro de Investigaciones Medicas Albert Einstein Fundacion-CIMAE, Buenos Aires, 1416, Argent.
SOURCE: Developmental Brain Research (2000), 120(1), 83-86
CODEN: DBRRDB; ISSN: 0165-3806
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the present study was to determine the developmental pattern of progesterone metabolism in rat brain and spinal cord from embryonic day 13 (E13) to the perinatal period. A marked decrease in the 5α-reduction of

progesterone in brain cortex was observed between E13 and postnatal day 5 (P5). Isopregnanolone was the predominant isomer in E13 in both cortex and spinal cord and its synthesis diminished gradually, while the concentration of allopregnanolone did not change significantly during development. The placental tissue was able to synthesize the 3α and 3β isomers in E13, E16 and E19 embryos with allopregnanolone being the major metabolite in all the samples. We conclude that embryonic central nervous system tissues are able to synthesize neurosteroids at least from stage E13 and that they are developmentally regulated.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 22 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:746730 CAPLUS
DOCUMENT NUMBER: 132:73803
TITLE: Sex-Dependent Behavioral Effects of the Neurosteroid Allopregnanolone (3α,5α-THP) in Neonatal and Adult Rats after Postnatal Stress
AUTHOR(S): Zimmerberg, B.; Rackow, S. H.; George-Friedman, K. P.
CORPORATE SOURCE: Bronfman Science Center, Department of Psychology, Williams College, Williamstown, MA, USA
SOURCE: Pharmacology, Biochemistry and Behavior (1999), 64(4), 717-724
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The neuroactive steroid allopregnanolone (3a-hydroxy-5a-pregnan-20-one, 3α,5α-THP) has been shown to be involved in the central nervous system's response to stress. This experiment investigated whether response to the neuroactive steroid allopregnanolone, a pos. modulator of the GABAA receptor, would be altered in neonatal or adult rats previously exposed to a chronic stressor-daily maternal separation during the first week of life. Subjects were then tested either as neonates or adults. In neonates, allopregnanolone decreased the number of ultrasonic vocalizations after brief maternal separation Previously separated subjects vocalized less and were less active than controls, but were not more sensitive to allopregnanolone on either measure. In adulthood, subjects with a prior history of maternal separation had a greater grooming response to a novel environment after a 10-min cold water swim test than nonsepd. subjects. Allopregnanolone reduced grooming, but, again, there was no difference due to stress history. A significant effect of gender was noted in the adult subjects-females were largely responsible for the effects reported. These results suggest that early maternal separation stress can produce an habituation response in neonates and a long-term sensitization response to later novel stress in adults. However, because the behavioral effects of allopregnanolone were not differentially influenced by this early stress history, the neuroactive steroid/GABAA receptor complex may not be the major mediator of these early stress sequela. Results indicating that females were more responsive to allopregnanolone than males are discussed in light of previous findings.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 23 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:709754 CAPLUS
DOCUMENT NUMBER: 132:10921
TITLE: Synaptic membrane freezing affects modulatory sites in avian central nervous system GABAA receptor

AUTHOR(S): Viapiano, Mariano S.; Gil, Diego J. Rodriguez; De Novara, Alba M. Mitridate; De Plazas, Sara Fiszer
CORPORATE SOURCE: Instituto de Biologia Celular y Neurociencias, Facultad de Medicina Universidad de Buenos Aires, Buenos Aires, 1121, Argent.
SOURCE: Neurochemical Research (1999), 24(11), 1347-1355
CODEN: NEREDZ; ISSN: 0364-3190
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies were carried out to determine whether barbiturates and neurosteroids share common recognition sites at the GABAA receptor complex in avian CNS. To achieve this, differentially prepared fresh and frozen synaptic membranes were used. Both the barbiturate, pentobarbital, and the neurosteroid, 3α-hydroxy-5α-pregnan-20-one, were able to stimulate GABA binding in both types of membranes. Stimulation differed markedly when both drugs were added jointly to different treated tissue. In frozen membranes drugs acted synergistically and were differentially displaced by picrotoxinin, while in fresh ones, where both compds. were inhibited by the convulsant, this additivity was absent. Post-freezing wash supernatants were collected and used as a source of putative endogenous factors involved in the above mentioned membrane differences. Addition of a high mol. weight fraction from supernatants to frozen synaptic membranes led to an inhibition of barbiturate and neurosteroid potentiation, as well as a loss of their additive effect. The authors' results indicate that GABAA receptor modulation by barbiturates and neurosteroids is affected by synaptic membrane treatment, with a common modulatory site in fresh membranes and sep. recognition sites after a freeze-thawing procedure. There may also be endogenous factors involved in overlapping of modulatory sites, which would thus regulate GABAA receptor functionality by direct interaction with the complex.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 24 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:689631 CAPLUS
DOCUMENT NUMBER: 132:73727
TITLE: Neurosteroids: pharmacology and physiological implications in behavior
AUTHOR(S): Akwa, Yvette; Baulieu, Etienne-Emile
CORPORATE SOURCE: INSERM U488 Steroides, INSERM U488 Steroides et Systeme Nerveux, Le Kremlin-Bicetre, 94276, Fr.
SOURCE: Journal de la Societe de Biologie (1999), 193(3), 293-298
CODEN: JDSBFG
PUBLISHER: SGS
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB A review, with 27 refs. The term "neurosteroids" applies to those steroids that are both formed in the nervous system from sterol precursors, and accumulate in the nervous system, at least in part, independently of peripheral steroidogenic glands secretion. Neurosteroids, that are active on the central nervous system include, mainly, pregnenolone (PREG), dehydroepiandrosterone (DHEA) and their sulfate esters (PREG-S and DHEA-S), as well as the reduced metabolite of progesterone, 3α,5α-TH PROG also called allopregnanolone. These neuroactive neurosteroids alter neuronal excitability by modulating the activity of several neurotransmitter receptors and thus can influence behavior. PREG-S decreases the sleeping time in rats anesthetized with a barbiturate, which is consistent with its antagonist action on the GABAA receptor (GABAA-R). Allopregnanolone is anxiolytic in rats tested in a conflict paradigm, through an interaction at a site specific

for the benzodiazepine (BZ) receptor inverse agonist RO15-4513 and/or at the picrotoxinin site on GABAA-R. The contribution of the amygdala, a key region involved in the control of anxiety, is also demonstrated for the anxiolytic action of allopregnanolone. An anti-aggressive effect of DHEA can be observed in castrated male mice who become aggressive in the presence of lactating females. This inhibition of aggressiveness by DHEA is associated to a selective decrease in the brain of PREG-S, which may, in turn, trigger an increase of endogenous GABAergic tone. Finally, cognitive performances of aged rats tested in the Morris water maze and the Y-maze can be correlated with individual concns. of PREG-S in the hippocampus, i.e poor performance in both tasks with low levels of PREG-S. Remarkably, the memory deficits are significantly improved, albeit transiently, by an intra-hippocampal injection of PREG-S in impaired aged rats. Promnesiant PREG-S may then reinforce some neurotransmitter systems that can decline with age. This brief review provides evidence of the pharmacol. and physiol. correlates of neurosteroids involved in behavioral phenomena. However, neurobiol. mechanisms of behavioral effects of neurosteroids await further investigation.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 25 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:437559 CAPLUS

DOCUMENT NUMBER: 131:197313

TITLE: Androgen-activating enzymes in the central nervous system

AUTHOR(S): Poletti, Angelo; Martini, Luciano

CORPORATE SOURCE: Istituto di Endocrinologia, Universita di Milano, Milan, 20133, Italy

SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1999), 69(1-6), 117-122
CODEN: JSBBEZ; ISSN: 0960-0760

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A discussion and review with 48 refs. In the rat brain, several steroids can be converted by specific enzymes to either more potent compds. or to derivs. showing new biol. effects. One of the most studied enzyme is the 5α-reductase (5α-R), which acts on 3-keto-Δ4 steroids. In males, testosterone is the main substrate and gives rise to the most potent natural androgen dihydrotestosterone. In females, progesterone is reduced to dihydroprogesterone, a precursor of allopregnanolone, a natural anxiolytic/anesthetic steroid. Other substrates are some gluco- and minero-corticoids. Two isoforms of the 5α-R, with limited degree of homol., have been cloned: 5α-R type 1 and type 2. The 5α-R type 1 possesses low affinity for the various substrates and is widely distributed in the body, with the highest levels in the liver; in the brain, this isoform is expressed throughout life and does not appear to be controlled by androgens. 5α-R type 1 in the rat brain is mainly concentrated in myelin membranes, where it might be involved in the catabolism of potentially neurotoxic steroids. The 5α-R type 2 shows high affinity for the various substrates, a peculiar pH optimum at acidic values and is localized in androgen-dependent structures. In the rat brain, the type 2 isoform is expressed at high levels only in the perinatal period and is controlled by androgens, at least in males. In adulthood, the type 2 gene appears to be specifically expressed in localized brain regions, like the hypothalamus and the hippocampus. The 5α-R type 2 is present in the GT1 cells, a model of LHRH-secreting neurons. These cells also contain the androgen receptor, which is probably involved in the central neg. feedback effect exerted by androgens on the hypothalamic-pituitary-gonadal axis. The physiol. significance of these and addnl. data will be discussed.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L15  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:293431  CAPLUS
DOCUMENT NUMBER:          136:304454
TITLE:                    Methods for the treatment of a traumatic
                          central nervous system
                          injury
INVENTOR(S):              Stein, Donald Gerald; Hoffman, Stuart Wayne
PATENT ASSIGNEE(S):       Emory University, USA
SOURCE:                   PCT Int. Appl., 52 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2002030409         A2    20020418    WO 2001-US31705         20011010
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002072509         A1    20020613    US 2001-973375          20011009
     CA 2425650            AA    20020418    CA 2001-2425650         20011010
     AU 2002011612         A5    20020422    AU 2002-11612           20011010
     EP 1365752            A2    20031203    EP 2001-979677          20011010
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004532796         T2    20041028    JP 2002-533852          20011010
     US 2005187188         A1    20050825    US 2005-85889           20050322
PRIORITY APPLN. INFO.:                       US 2000-239505P      P  20001011
                                             US 2000-245798P      P  20001103
                                             US 2001-973375       A  20011009
                                             WO 2001-US31705      W  20011010
AB   The invention provides methods for conferring a neuroprotective effect on
     a population of cells in a subject following a traumatic injury to the
     central nervous system.  Specifically, the methods of the invention
     provide for the administration of a progestin or progestin metabolite
     following a traumatic brain injury.  The progestin or progestin metabolite
     is administered at therapeutically effective concns. that produce a
     neuroprotective effect (i.e., a decrease in the loss of neuronal activity)
     and reduces and/or prevents the various physiol. events leading to
     neurodegeneration, such as, cerebral edema and the immune/inflammatory
     response.


=> s CNS disorders
L16       2931 CNS DISORDERS

=> s L6 and L16
L17          6 L6 AND L16

=> dup rem L17
PROCESSING COMPLETED FOR L17
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L18 6 DUP REM L17 (0 DUPLICATES REMOVED)

=> d 1-6 ibib abs

L18 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:494872 CAPLUS
DOCUMENT NUMBER: 145:100655
TITLE: Action by and sensitivity to neuroactive steroids in menstrual cycle related CNS disorders
AUTHOR(S): N-Wihlbaeck, Anna-Carin; Sundstroem-Poromaa, Inger; Baeckstroem, Torbjoern
CORPORATE SOURCE: Umea Neurosteroid Research Center, Department of Clinical Sciences, University of Umea, Umea, Swed.
SOURCE: Psychopharmacology (Berlin, Germany) (2006), 186(3), 388-401
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Neuroactive steroids are a large group of substances having effect in the brain and on brain function. The steroids most studied are allopregnanolone (ALLO), tetrahydrodeoxycorticosterone (THDOC), pregnenolone sulfate (PS) dihydroepiandrosterone sulfate (DHEAS), and estradiol (E2). ALLO and THDOC are called gamma-aminobutyric acid (GABA) steroids as they are pos. modulators of the GABAA receptor in a similar way as benzodiazepines, barbiturates, and alc. GABA steroids not only have similar behavioral effects as benzodiazepines and barbiturates but, possibly, also similar adverse effects as well. This review aims to elucidate the possible role that neuroactive steroids play in the development of mood disorders in women. One of the most clear-cut examples of the interaction between mood, neuroactive steroids, and the GABA system is premenstrual dysphoric disorder (PMDD), which is a cluster of neg. mood symptoms occurring during the luteal phase of the menstrual cycle in 2-6% of reproductive women. Furthermore, certain women also experience adverse mood effects during sequential progestin addition to postmenopausal estrogen treatment, which is why the role of neuroactive steroids in postmenopausal women is also addressed in this review.
REFERENCE COUNT: 170 THERE ARE 170 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1220692 CAPLUS
DOCUMENT NUMBER: 143:477643
TITLE: Preparation of enaminones as modulators of GABAA and nicotinic acetylcholine receptors
INVENTOR(S): Hogenkamp, Derk J.; Johnstone, Timothy B. C.; Gee, Kelvin W.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005108347	A2	20051117	WO 2005-US15869	20050505
WO 2005108347	A3	20060706		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,

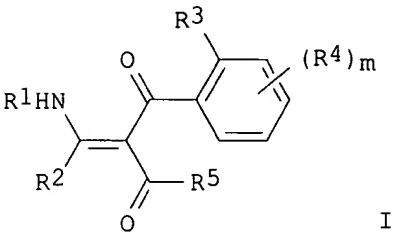
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

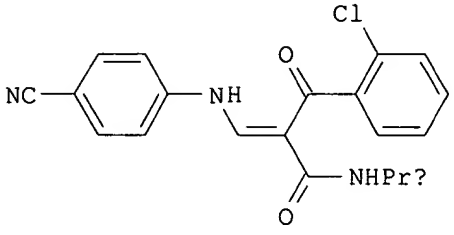
PRIORITY APPLN. INFO.: US 2004-569465P P 20040506

OTHER SOURCE(S): MARPAT 143:477643

GI



I



II

AB Title compds., such as I [wherein R1 = (un)substituted (hetero)aryl, aralkyl, etc.; R2 = H or (un)substituted alkyl; R3, R4 = halo, alkoxy, nitro, etc.; R5 = (un)substituted alkyl, alkoxy, amino, etc.; m = 0-4, with limitations, and pharmaceutically acceptable salts, prodrugs or solvates thereof] were prepared as modulators of GABAA and nicotinic acetylcholine receptors. For instance, 2,2-dimethyl-1,3-dioxane-4,6-dione underwent condensation successively with 2-chlorobenzoyl chloride in the presence of DMAP, propylamine, N,N-dimethylformamide dimethylacetal and 4-(trifluoromethyl)aniline to give II. Several biol. assays were executed. Representative I showed inhibition against GABA receptor with IC50 of 0.01 - 0.20 μM in the (35S)-TBPS binding assay. Therefore, the invented compds. and their pharmaceutical compns. are useful for the treatment of CNS disorders amenable to modulation of GABAA and nicotinic acetylcholine receptors.

L18 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:570823 CAPLUS

DOCUMENT NUMBER: 139:112167

TITLE: Pregnane steroids for use in the treatment of steroid-related CNS disorders

INVENTOR(S): Baeckstroem, Torbjoern; Lundgren, Per; Wang, Ming-de; Johansson, Inga-maj

PATENT ASSIGNEE(S): Umecrine Ab, Swed.

SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059357	A1	20030724	WO 2002-SE2423	20021220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2468248	AA	20030724	CA 2002-2468248	20021220
AU 2002359202	A1	20030730	AU 2002-359202	20021220
EP 1458399	A1	20040922	EP 2002-793723	20021220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1607954	A	20050420	CN 2002-826275	20021220
JP 2005519893	T2	20050707	JP 2003-559519	20021220
US 2005222099	A1	20051006	US 2005-499214	20050428
PRIORITY APPLN. INFO.:			SE 2001-4423 A	20011227
			WO 2002-SE2423 W	20021220

AB Steroid compds. possessing a hydrogen donor in 3β position, either in the form of a hydroxy- or a sulfate group, function as efficient blockers of the 3α-hydroxy-pregnane-steroid action and thus have utility as therapeutic substances for the prevention and/or treatment of steroid related CNS disorders. Treatment methods based on the administration of these substances are disclosed, and these substances either alone or in combination are also suggested for the manufacture of pharmaceuticals for the treatment of many specific steroid induced CNS disorders.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:254293 CAPLUS
DOCUMENT NUMBER:	140:389275
TITLE:	Pathogenesis in menstrual cycle-linked CNS disorders
AUTHOR(S):	Baeckstroem, Torbjoern; Andersson, Agneta; Andree, Lotta; Birzniece, Vita; Bixo, Marie; Bjoern, Inger; Haage, David; Isaksson, Monica; Johansson, Inga-Maj; Lindblad, Charlott; Lundgren, Per; Nyberg, Sigrid; Oedmark, Inga-Stina; Stroemberg, Jessica; Sundstroem-Poromaa, Inger; Turkmen, Sahruh; Wahlstroem, Goeran; Wang, Mingde; Wihlbaeck, Anna-Carin; Zhu, Di; Zingmark, Elisabeth
CORPORATE SOURCE:	Umea Neurosteroid Research Center, Department of Clinical Sciences, Obstetrics and Gynecology, Norrlands University Hospital, Umea, SE-901 85, Swed.
SOURCE:	Annals of the New York Academy of Sciences (2003), 1007(Steroids and the Nervous System), 42-53 CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER:	New York Academy of Sciences
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. That 3α-hydroxy-5α/β-pregnane steroids (GABA steroids) have modulatory effects on the GABA-A receptor is well known. In behavioral studies in animals high exogenous dosages give concns. not usually reached in the brain under physiol. conditions. Animal and human studies show that GABA-A receptor-pos. modulators like barbiturates, benzodiazepines, alc., and allopregnanolone have a bimodal effect. In pharmacol. concns. they are CNS depressants, anesthetic, antiepileptic, and anxiolytic. In low dosages and concns., reached endogenously, they can induce adverse emotional reactions in up to 20% of individuals. GABA steroids can also induce tolerance to themselves and similar substances, and rebound occurs at withdrawal. Menstrual cycle-linked disorders can be understood by the concept that they are caused by the action of endogenously produced GABA-steroids through 3 mechanisms: (a) direct action, (b) tolerance induction, and (c) withdrawal

effect. Examples of symptoms and disorders caused by the direct action of GABA steroids are sedation, memory and learning disturbance, clumsiness, increased appetite, worsening of petit mal epilepsy, neg. mood as tension, irritability and depression during hormone treatments, and the premenstrual dysphoric disorder (PMDD). A continuous exposure to GABA steroids causes tolerance, and women with PMDD are less sensitive to GABA-A modulators. A malfunctioning GABA-A receptor system is related to stress sensitivity, concentration difficulties, loss of impulse control, irritability, anxiety, and depression. An example of withdrawal effect is "catamenial epilepsy," when seizures increase during menstruation after the withdrawal of GABA steroids. Similar phenomena occur at stress since the adrenal produce GABA steroids during stress.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:730545 CAPLUS
DOCUMENT NUMBER: 137:242465
TITLE: Method and compounds for use in the treatment of steroid induced states of the central nervous system
INVENTOR(S): Backstrom, Torbjorn; Wang, Ming-De
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 37,869, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6455516	B1	20020924	US 1999-266035	19990311
PRIORITY APPLN. INFO.:			US 1998-37869 B2	19980311

OTHER SOURCE(S): MARPAT 137:242465
AB The use of epiallopregnanolone (3β-hydroxy-5α-pregnan-20-one) for the treatment of steroid induced mood disorders and CNS disorders is disclosed. Further, the use of epiallopregnanolone for the manufacture of pharmaceuticals is disclosed, together with an list of symptoms suitable for treatment with epiallopregnanolone.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:594945 CAPLUS
DOCUMENT NUMBER: 131:209578
TITLE: Epiallopregnanolone in the treatment of CNS disorders, mood disorders, and tiredness and for the control and termination of steroid anesthesia
INVENTOR(S): Backstrom, Torbjorn; Wang, Ming-de
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945931	A1	19990916	WO 1999-EP1496	19990310

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,

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CA 2321728	AA	19990916	CA 1999-2321728		19990310
AU 9933292	A1	19990927	AU 1999-33292		19990310
AU 756001	B2	20030102			
EP 1063999	A1	20010103	EP 1999-914491		19990310
EP 1063999	B1	20051026			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002506034	T2	20020226	JP 2000-535346		19990310
AT 307592	E	20051115	AT 1999-914491		19990310
PRIORITY APPLN. INFO.:			US 1998-37869	A	19980311
			WO 1999-EP1496	W	19990310

AB The use of epiallopregnanolone (3β-hydroxy-5α-pregnan-20-one) for the treatment of inter alia steroid induced mood disorders and CNS disorders, for the control and termination of steroid anesthesia, and for the prevention of tiredness. Further, the use of epiallopregnanolone for the manufacture of pharmaceuticals is disclosed, together with a list of symptoms suitable for treatment with epiallopregnanolone or pharmaceuticals comprising the same.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT